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GENERAL PARALYSIS IN TWO SISTERS, COMMENCING AT THE AGE OF TEN AND FIFTEEN RESPECTIVELY.—AUTOPSY IN ONE CASE.[1]

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GENERAL paralysis in early life, i. e., under the age of twenty, has, so far as I can see from the literature, not been reported in this country; in fact, altogether I can find no more than about fifty cases, among which certainly thirty-five have been described since the year 1890, and over twenty in the last two years. Among all the cases about the same number, i. e., twenty, have been described by English and German observers. About seven cases are found in the French and a few in the Russian literature.[2]

The two cases to be reported may, therefore, prove of interest, particularly since they represent the occurrence of the disease in two members of the same family, particularly, also, since the autopsy in one of our cases showed changes which by themselves I consider of special interest.

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[1] From the laboratory of the McLean Hospital, Waverly, Mass.

[2] For a complete bibliography up to 1895, see article of Alzheimer: "Die Frühformen der allgemeinen progressiven Paralyse."—Allgemeine Zeitschrift für Psychiatrie, etc., Vol. LII., page 533.

The cases are typical, and by the examination of the nervous system the diagnosis is raised above all doubts. The younger sister I have not observed myself. She was under the care of Dr. Cushing, in Haverhill, who furnished me with some information; the bulk of the history, however, I got by collecting the data from the different members of the family whom I went to see. The clinical picture can, therefore, not be expected to be in any way complete, and the following description will only give in a very general way the course of the disease.

Case I.—Ida. The patient was healthy as a baby and, according to the statement of different members of her family, in every way normal. She was even considered a very bright child, whereas her sister, whose case is to be spoken of later, is said to have been of moderate average intelligence. The time of onset of her disease is difficult to fix and was certainly very gradual, but when the patient was about ten years old it was thought that she was growing lazy. Instead of playing with other children she would sit around the house in an apathetic way. She frequently complained of pain about her stomach, but had no vomiting. On account of this trouble she is said to have been kept out of school. When about 11 years of age she began to have marked motor symptoms, staggered about a good deal " like a drunken man," and on that account she had to be guided around. One of my informants, her sister, expressed the course of the disease with reference to the motor symptoms in short as follows: " Two years we dragged her around, two years she sat in a chair and two years she was in bed." From about fourteen years the patient's legs had a tendency to be drawn up, and while the patient was in bed in the latter part of her life this became so marked that even passive extension was difficult. Later a similar condition appeared in the arms and toward the end they were drawn over the chest. For the last two years it was impossible for the patient to sit up in a chair. The voice was noticed to be coarser than it had been and the speech to be indistinct; towards the end of the patient's life it was nothing but a mumble. In the meantime the mental condition approached more and more a complete dementia, and for about a year before death the patient was so feeble-minded that she knew no one. She lay in bed in the above described contracted condition, untidy, mumbling, picking at her bed-clothes, unable to help herself in any way. The course was apparently one of progressive dementia without any excitement or any delusions. At no time during the course were any convulsions noted until shortly before death when she had a series of them. She died in convulsions a week after their onset.

The autopsy was made by Dr. E. W. Taylor in the presence of Dr. Putnam. To the former I am indebted for the description of the gross appearances of the nervous system; to Dr. Putnam it is my privilege here to express my indebtedness, not only for the pathological material which he put at my disposal, but, also, for drawing my attention to these cases. It was with him that I first saw the sister who is now living. In this place I would also express my thanks to Dr. Cowles for his kindness in admitting the latter to this hospital.

Before giving the anatomical details gained from a study of the tissues, I wish to give an abstract of the clinical notes made on the sister whom we had in the hospital, as well as give some data with reference to the family history.

Case II.—Rosa, now nineteen and a half years old, has been a healthy child and of average intelligence up to the onset of the present disease; for the latter there is no cause to be made out. From her fifteenth year on she got along badly in school, and since about her sixteenth year she has been, even according to the judgment of her family, feeble minded. She has never had any excitement nor any delusions or hallucinations. Her mental weakness was first shown in an inability to follow school work, then in lack of interest in anything, in a certain childishness, in a loss of memory and, finally, in an inability to understand even the simplest things. To give an example: she has for the last few years very frequently done crochet work, always using the same stitch; the most painstaking attempts on the part of her sister to teach her even the slightest modification of this were fruitless. For two or three years her gait has been changed and she is somewhat uncertain. Her speech also became altered, the change coming on gradually. She has had no convulsions. This is, in short, the history up to the time I saw her. The observations which on frequent occasions were made during her stay in the hospital, i. e., during about five months may be summed up as follows (to give a resumé of the notes made is particularly easy since the change has not been great; no new symptoms have appeared, but she has become somewhat more demented, her walk more uncertain, her tremors more marked): She is distinctly feeble-minded; after her arrival, although she had been told that she was coming to this hospital, she was not clear where she was; she was satisfied at once and when her sister left her she did not mind it. Afterwards she frequently cried and said she was homesick, but a few words completely changed her feelings, which were evidently but very superficial. In spite of being in a rather noisy ward, associated with persons with many marked peculiarities, this did not disturb her or make any impression upon her; in other words she was, although quiet and orderly, absolutely unable to appreciate her surroundings. A picture was shown to her, and her description of it, which she was asked to give, was very elementary and superficial; her behavior was often silly. During an examination she would often tell of a perfectly irrelevant incident which had happened in her neighborhood, or laugh convulsively. She was able to recite fairly well a number of poems she had learned when in school, but it was evident she had hardly grasped the meaning of them. Thus it happened that she left out lines and words without noticing it, making the meaning incomprehensible. On several occasions the patient was asked to read, and the results here obtained were quite characteristic. From a number of tests made on different occasions I shall only give a general abstract. She was asked to read a paragraph from "Alice in Wonderland." She made mistakes like the following: Instead of unfortunate she read uniform; for execution, express; for sneezing, snize; for choking, colking; for lizzard, laze, and other similar errors; while many words were also read correctly. Individual letters could always, smaller words almost always, be correctly read when shown alone, sometimes only after spelling, e. g., mock, fashion. Longer words, like squeaking or even turtle, could not be read, even after spelling; in the same way words which probably she had never heard or seen, like gryphon or guinea pig, could be spelled, but no attempt was made to pronounce them. Figures could be read alone or two or three together, frequently even four, but never more. Writing was difficult to obtain, since the patient could not be made to write much, but the few specimens show not only mental defects analogous to those expressed in reading, but, also, very marked motor disturbances, i. e., tremulousness. To anyone familiar with the subject her handwriting would at once have suggested general paralysis. She calculated very badly and, with the exception of the smallest multiplications, with two or three, possibly four, she did not give correct answers. Multiplication she did better than addition or division. This is evidently due to the fact that the multiplication tables have by practice become more fixed associations than the additions or divisions. She evidently depended entirely on some well-rooted associations, for where examples with any higher figures, as e. g., 5x6 or 13—11, were given to her, she not only did not do them at once, but knew no means of getting at the results; in other words, no matter how long a time was given to her to solve the problem she never reached a solution. Quite a large number of tests were made, and the patient, both of her own accord and with the assistance of the nurse, attempted frequently to write down the multiplication tables. She improved her calculation hardly any by this practice. It should be emphasized here once more that the patient was in school up to her fifteenth year and had been perfectly able to read, write and calculate. Rieger and his pupils have pointed out that disturbances like these, if at all pronounced, are very characteristic of the dementia of general paralysis.

The gait was markedly abnormal. It was tottering, the legs placed far apart and held somewhat stiffly; the feet came down on that account somewhat as in a flat-footed person. She wavered much from a straight line. The arms, during walking, were held away from the body as if for balancing the latter. She can stand with her eyes closed and feet close together, but cannot stand on one foot at all. The speech is indistinct, monotonous, high-pitched, and has a certain vibration to it; frequently words are somewhat slurred over; at the same time there is a coarse tremor about the mouth and chin and a similar tremor is seen in the tongue. The face is somewhat one-sided; this is seen at rest as well as in motion. The patellar reflexes have been throughout markedly exaggerated and there has been on different occasions a more or less well marked patellar clonus but only a slight ankle clonus. The reflexes in the arms were increased, particularly during the latter part of her stay in the hospital. The pupils have been the same all along. The right was larger than the left on every examination, and neither eye reacts to light or accommodation.

The condition of the sensibility is of interest. She perceives tactile impressions very well, but there is marked diminuition in her appreciation of pain sensations. At first she not rarely failed to recognize the pin as such; when her attention was drawn to it she frequently differentiated the head and the point of the pin correctly, but she never minded the pain; in fact, a fold of skin could be transfixed without her wincing. The same thing was seen in applying the faradic or galvanic current of full strength; it was borne without pain, even if the metal of the electrode was directly applied.

The patient shows no signs of hereditary syphilis. The upper teeth are badly decayed, those left are not Hutchinsonian, the corneae are clear, the shins smooth, the liver-dulness normal.

So much for the clinical history of the second patient.

Family History—These two girls are the youngest members of a family of 7 children. The others are healthy and normal. None show signs of hereditary syphilis. None have died except Ida. The mother had no miscarriages.

The father, a Dane, has been unable to work for about twelve years, although he is now only sixty-one years old. He frequently became dizzy and was said to be unable to direct his hands properly. Six years ago he had an attack in which he got pale, fell down and was weak on one side. He recovered completely. He now falls not infrequently, partly, as he says, because he becomes dizzy, partly because he stumbles. He is said to have had frequently sores break out over his body, and last year two "boils" appeared on the forehead, which were present most of the summer; they finally broke open and dead bone was found in them. At the same time he had a good deal of headache. He is irritable, but has been so for years. Never does any work, but sits about the house, perhaps reading in his old Danish Bible. He denies positively ever to have had any syphilis. On examining the man I found him looking certainly older than he was and quite infirm. There was a tremor of the head from side to side, a tremor of the muscles about the face when he spoke, but the speech was not altered. There was a certain amount of difference in the two sides of the face. Tongue protruded straight and did not tremble. He has some tremor of the hands and the handwriting is tremulous. The muscular strength of the arms and legs is fair and equal on the two sides. The gait is very infirm and tottering, but not ataxic; it became worse when his eyes were closed, but he stood very well with his eyes closed. The knee-jerks are diminished. No changes are seen about the eyes, the pupils react to light and distance. On the forehead there are two deep ragged scars and there is evidently loss of bone. His arteries are somewhat thickened.

I do not see that we can make a definite diagnosis in this patient; he certainly has not general paralysis. The most likely explanation seems to me—to be sure after too short a period of observation—that the man is prematurely senile; he has a certain amount of arteriosclerosis. That the man had syphilis is made probable by the appearance of the two "boils" on the forehead.

The mother, also, is infirm and complains of all sorts of pains. She dates her troubles from the sickness of her daughter, whom she nursed. Examination was negative. She is intelligent and seems merely nervous and hysterical.

Autopsy on Case No. I—(Dr. Taylor)—Dec. 1, 1894. Girl sixteen years old. Size of body, that of a child of ten years of age; body emaciated. Lower legs particularly thin and emaciated in comparison to the body, where there is considerable subcutaneous fat. The head is well formed; no deformity.

Slight erosion of the inner table of the skull on the left side; normal thickness of skull. Dura mater is normal. Considerable serous fluid runs out on removal of the skull-cap. The pia mater is opaque and milky in appearance, especially over the sulci. The brain substance is firm on pressure. The convolutions are very pale and bloodless and the substance firm on section. The cortex is considerably thinner than normal. There is considerable fluid in the ventricles. The pons, medulla and spinal cord show no abnormality macroscopically.

The internal organs are normal. The uterus is very undeveloped.

Microscopical Examination.—Microscopically there were examined different sections of the brain cortex, portions of the cerebellum of the basal ganglia and different levels of the pons, medulla and spinal cord.

The cortex shows the changes commonly found in general paralysis. The pia is thickened and there is great infiltration with lymphoid cells. With reference to the ganglionic cells little can be said. The tissues were hardened in Müllers fluid[3] but the cells were not well preserved. With a low power the most striking feature in the cortex everywhere is the meshy appearance in many places, which is most marked in the most superficial layer. We note also wide spaces around the blood vessels and around nerve cells, the apparently increased number of nuclei throughout the tissue and the great infiltration of the adventitial spaces with lymphoid cells. All the vessels are very conspicuous on this account. With the high power the most striking feature is the large number of coarse spider cells, which are very evident in the superficial and deep portions of the cortex, especially in the lower portions they are more pronounced than is commonly seen in general paralysis. They are often very coarse and can be distinctly seen with a low power. The bodies of these cells are often quite large and stained deeply with fuchsin. In the white matter also spider cells are seen and, as it seems, they are more numerous the nearer one gets to the cortex.

The medullated nerve-fibres appear much diminished, not only the tangential fibres in the superficial layer which with the exception of a few places in the occipital lobes, are almost entirely lost, but, also, the horizontal fibres lower down and even the radial. This diminution is very great and very widespread. It may be due to the staining method, but, on the one hand. the change was well marked in the coarser fibres, and, on the other hand, the fibres in the white matter were well stained, although distinctly diminished in many places. It should also be remembered that the patient began to become affected with the disease very early in life, at a time when the cortex does not show all the fibres which it has in mature life.[4] The changes on the whole were very pronounced and well marked all over the cortex, although less marked in the posterior than in the anterior regions.

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[3] The tissues were stained by Weigert's method and with Alum-Haematoxylin and a dilute watery solution of Fuchsin.

In sections from the optic thalamus very similar changes were seen as in the cortex; here, also, large, sometimes huge, spider-cells were found, and the vessels showed large accumulations of lymphoid cells. The latter condition, in fact, was seen all through the nervous system, no matter what portion was looked at. But, aside from this, the vessel walls looked normal with the exception of a few places in the basal ganglia, where there was distinct hyaline degeneration of vessels and where amyloid bodies were seen.

In the cerebellum the pia also showed thickening and marked infiltration with lymphoid cells. The changes in the cortex are interesting. In places it is perfectly normal, the Purkinje cells well formed with well stained nuclei, the layer above them homogeneous looking. In other places there are marked changes, the cells look hyaline, deeply stained with fuchsin with ragged outlines, misshapen, and with nuclei that stained very deeply and evenly and which presented irregular outlines. These changes were seen in different regions in different degrees and in places the Purkinje cells had completely disappeared. Where these alterations are seen the entire cortical substance is much changed; it has a fibrillary appearance instead of the normal homogeneous one, the fibres are coarse and chiefly directed vertically, although many are oblique and horizontal, the latter particularly in the most superficial portion where they form a dense layer. Well marked spider cells are seen, especially in the most profoundly altered portions, and the whole thickness of the cortex is more or less reduced. We have here a great increase of neuroglia, which has, no doubt, followed the degeneration of the Purkinje cells with their great branching systems.

The uneven distribution of the changes is quite striking, and it is of interest to note that the affected parts are chiefly in the periphery of the organ, whereas the deeper portions are usually normal.

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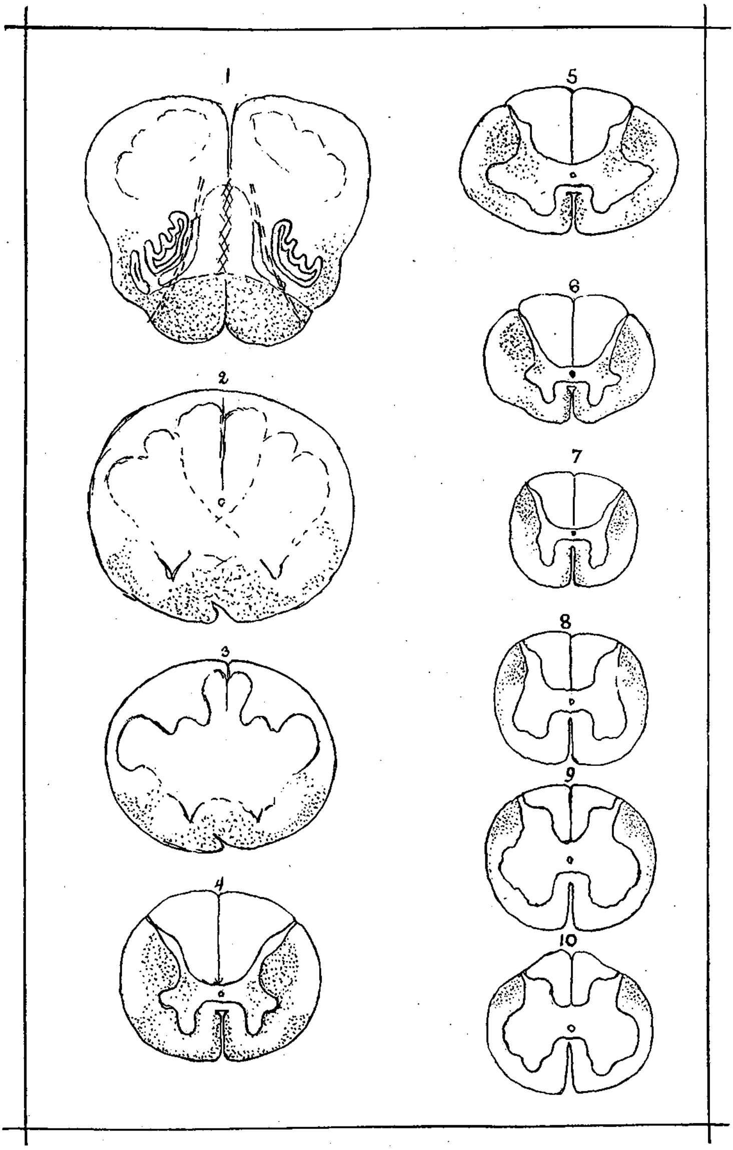
[4] Cf. Vulpius: Ueber die Entwickelung und Ausbreitung der Tangentialfasern des menschlichen Grosshirns während verschiedener Altersperioden. Arch. f. Psychiatrie. Band xxiii (1892), p. 775.

Spinal Cord.—In the sacral cord there is degeneration, chiefly confined to the lateral pyramidal tracts, although it extends evidently also somewhat inward (Fig. 10).

In the lumbar cord the same condition is found, namely, the degeneration of the lateral pyramidal tracts; here it extends, perhaps, somewhat ventrally along the periphery of the cord. As we ascend, the field of degeneration approaches nearer to the gray matter, whereas at the periphery it is less pronounced, this corresponds again to the position of the lateral pyramids, while there is also a certain amount of degeneration along the margin (Fig. 8). In the dorsal cord we begin to see with certainty a degeneration in the field of the anterior pyramidal tracts; the light appearance in the lateral columns (in Weigert sections) is well marked, but not quite confined to the pyramidal tracts; it extends forward, although it is better marked in the former region. It must be stated that at no place is there anything like a complete degeneration in the lateral pyramidal tracts, but the changes in a Weigert section are clearly enough marked to be very well seen with the naked eye. The field of the direct cerebellar and of Gowers' tracts is entirely free from degeneration. In the upper dorsal cord (Fig. 6) the direct cerebellar tract is well stained, but ventrally from it there is a distinctly lighter appearance, i. e., in the region of Gowers' tract. The degeneration in the lateral columns is well pronounced in the region of the pyramids, but shades off in a ventral direction and blends with the degeneration in the region of Gowers' tract; it also extends along the outer surface of the posterior horns and the pyramids degeneration is pres- the posterior horns and the pyramids degeneration is pres-ent, but not so well marked as in the region of the pyramids; so that in this direction also the degeneration is not quite confined to the lateral pyramids, although, again, it is more pronounced here. The anterior pyramids show distinct changes, particularly on one side, but these do not extend along the anterior border of the cord. Very similar is the condition in the cervical cord. The direct cerebellar tract is perfectly normal, the pyramidal degeneration shading off in a ventral direction and around the an-



DESCRIPTION OF THE PLATE.

The black dots indicate the regions of degeneration; in the gray matter of the spinal cord the dots indicate the great developement of spider cells.

terior horns, blending with the degeneration in the region of Gowers' tract, which has now become more pronounced. The anterior pyramids show here also more pronounced degeneration. As we go up still higher (Fig. 4), (the level of the accessorius), we find similar conditions. Here, however, there is a field of degeneration in the region of Gowers' tract which is more circumscribed and more pronounced than in any region below; it extends in a triangular projection towards the anterior horn and does not extend dorsally as far as the outgoing root of the accessorius, but only to a point which is about on a line with the ventral border of the lateral projection of the gray matter; interesting is also the fact that it extends inward and ventrally to the field of degeneration in the anterior pyramids, which here shows, unlike that lower down, a marked extension outward. The connection between this and Gowers' tract is well marked, but the degeneration here is only a small strip. It is necessary to state here that, unfortunately, the different levels were not marked, and that a large part of the cervical cord could not be examined, so that it is impossible to say where this more pronounced field of degeneration began.

As we ascend from here into the medulla, at a place where the nucleus of Goll is well formed, but the pyramidal decussation not yet finished (Fig. 3) we find the degeneration in the field of Gowers' tract well marked and having about the same place as lower down; it is connected by a strip with the degeneration in the pyramids, a strip which is distinctly separated from the periphery by normal-looking nerve fibres. There is also a slight degeneration extending from this well-marked field slightly dorsally and inward to the anterior horns. Still higher up, where both the nucleus gracilis and cuneatus are well formed, at the level of the sensory decussation, the degeneration is still in the same position, separated from the periphery by some longitudinally cut fibres and blending with that of the pyramids, which is still well marked; here, also, it extends inward. Still higher up, where the olive appears, we see in Weigert sections that the field adjoining the pyramids, namely, the region around the olive inside of the external arciform fibres, is considerably lighter than normal and in the angle just ventral to this region there is a somewhat lighter appearance than normal. Above this region, i. e., where the olive is well formed, the degeneration cannot be made out with certainty. The field situated in the angle at the external and dorsal side of the olive is light, but it is also so normally, so that a slight degeneration could probably anyhow not be made out easily, in Weigert sections, nor was it any more evident in fuchsin preparations. The pyramids are still seen to be partly degenerated. This latter degeneration can be followed through the medulla and partly through the pons; in the higher portion of the latter it becomes questionable, and in the crura cerebri it can no longer be made out.

The Gray Matter—There are here and there ganglionic cells in the anterior horns which are with certainty changed, having the same hyaline character as seen in the Purkinje cells described above; these changes are, perhaps, more marked in the dorsal cord. In the nuclei of the medulla and pons similar cells are found, but pronounced degeneration is found in none. As we stated above, the infiltration with lymphoid cells around the vessels is seen here as well as in other portions of the central nervous system. This is particularly well marked in some vessels in the pons. Another important alteration to be noted is the very marked changes in the gray matter of the spinal cord. We find in sections from the upper dorsal and the cervical cord a marked growth of neuroglia, which is seen in the appearance of numerous well-pronounced coarse spider cells which can be seen even with a low power. These cells are chiefly seen at the base of the anterior and posterior horns and in the centre of the gray matter on either sides, although isolated large neuroglia cells are also seen in other places. In the lower regions of the spinal cord this feature is not present. In the nerve roots as far as they were examined (those which were attached to the spinal cord sections) no changes were found.

Remarks on the Pathological Findings.—The changes in this case are very profound. They are well marked, not only in the cerebral cortex, but also in the basal ganglia, in the cortex of the cerebellum, and in the white and gray matter of the spinal cord and the medulla. With reference to the spinal cord the question arises how to interpret the changes which we have described. In the lateral as well as in the anterior columns we have seen a partial degeneration, confined in the latter to the anterior pyramids. Degeneration in the lateral columns is not an infrequent occurrence in general paralysis as is well known; it has of late been attributed by Pierre Marie in some cases to changes in the gray matter of the cord which gives rise to a degeneration of tract cells, and thus to loss of short tracts in this region. As reasons for this assumption the facts have been adduced that the degeneration is not confined to the lateral pyramids and is not present in the anterior pyramids. In our sections, however, we find throughout the entire length of the cord a degeneration which in some places is entirely confined to the lateral pyramids; in other places, though not limited, is certainly best marked in this region; besides it diminishes downward, pari passu, with the diminution of the pyramidal tracts. Moreover, we find a degeneration in the anterior pyramids which we can distinctly follow down the dorsal cord. All these are features which make the degeneration look like a secondary one due to cerebral changes; at any rate it is fair to say that we have before us a systemic degeneration in the central motor neurons, although the changes in the nerve fibres surrounding the pyramids must be attributed to degeneration of short tracts; in other words, the latter are not merely an extension of the process into the surrounding tissue, but are probably due to alterations in the gray matter of the cord. Whether, in spite of the appearances in the crura, there is a degeneration which is not evident in Weigert sections, or whether the process becomes really completely lost in the upper pons, is difficult to say. It is, however, possible that, as has been suggested by others, only the most peripheral portion of the neuron becomes first affected owing to its distance from its trophic centre and that gradually the process extends nearer to the latter. With gradual chronic changes and a slow degeneration of nerve cells as is the case in general paralysis this view is not improbable. I am inclined to see, therefore, in this degeneration of the pyramids a secondary effect of changes in the cortex.

With reference to the degenerated areas in the anterolateral region of the cord, there can hardly be any question but that we are dealing with degenerated fibres in Gowers' tract. It is noteworthy that this only appears in the upper portions of the cord, more particularly in the cervical region, becoming more pronounced as we ascend and very well marked in the upper cervical cord and the lower portions of the medulla. It cannot, however, be followed far up in the medulla; but this need not surprise us, because the fibres of Gowers' tract become rather scattered, and it would be difficult to see a partial degeneration in Weigert sections.

In view of the fact that Hoche[5] has demonstrated an anterior portion of Gowers' tract which extends to and along the anterior fissure, the question must naturally arise whether, perhaps, the degeneration along the anterior fissure and that in the antero-lateral region do not both belong to Gowers' tract; on the other hand, the fact that this anterior degeneration extends well into the dorsal cord a long distance below the antero-lateral degeneration and the fact that the degeneration of the pyramids is well marked in the medulla oblongata, i. e., before the separation of the anterior and lateral pyramids has taken place, speak against this, although it is not excluded that a part of the degeneration field really represents fibres belonging to the antero-lateral tract; indeed, this seems rather likely. High up in the cervical cord the degeneration in the antero-lateral region is continuous by a fine strip with the degeneration in the anterior pyramids and in the medulla the same is true, here particularly the degeneration extends further ventrally than the degeneration in Gowers' tract usually does as we observe it after sections of the cord. In one of Hoche's cases, however, where the lesion was high up (I. D.) the degeneration also extends further anteriorly. It is possible that the higher the lesion the further forward does the degeneration extend. Whether the well-marked loss of fibres around the olive represents in part at least fibres from Growers' tract or whether these are entirely different fibres is difficult to decide. The question which next arises is, What accounts for these degenerated fibres in Gowers' tract. According to Lenhossék[6] it is "probable" that the cells which give rise to the fibres of Gowers' tract are situated " partly in the centre of the anterior horns, partly in the central zone of the gray matter." We have seen that in the upper portions of the dorsal, more particularly in the cervical cord and here increasing as we advance upward, changes are found at the base of the anterior and posterior horns and in the centre of the gray matter on either side, indicated by a very marked increase of neuroglia. While to these changes we must probably in part attribute the degeneration in the ground bundles, it seems fair to suggest that the degeneration in Gowers' tract is also due to the destruction of cells in this region.

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[5] Cf. Hoche: Ueber secundäre Degeneration, etc. Arch. f. Psych., xxviii., Heft 2, p. 517.

[6] Der feinere Bau des Nervensystems im Lichte neuester Forschungen, 1895. p. 408.

Another feature of interest in these cases is the fact that two members of the same family were affected at this early age with this disease. I have been able to find this in only one other instance in the literature. These cases, reported by Justschenko,[7] are a brother and a sister, who were attacked by the disease at the age of fourteen and fifteen respectively. Both patients had signs of hereditary syphilis. Cases like these are qualified more than any others, it seems to me, to show how untenable is the idea that general paralysis is due to exhaustion and point to the rôle which hereditary influences play in the production of general paralysis at such an early age. It has been shown by Alzheimer,[8] who has collected forty-one cases of juvenile general paralysis, among them three of his own, that there was a neuropathic heredity in about seventy per cent., but the heredity which seems most important in these cases is syphilis. The same author finds that fifty per cent. had with certainty a syphilitic heredity; if those were added who had very probably such antecedents, the figures would rise to 85 per cent., and if still those were added in whom a syphilitic heredity was from certain data probable, to ninety-one per cent., an unusually high percentage. It is, of course, impossible to say definitely how many of these cases are in some way due to hereditary syphilis; but, considering the frequency of the association of the two, we may well keep in mind the interesting study of Hirschl,[8] who, in the attempt to prove syphilis

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Progressive Paralyse des Jugendalters. Russisches Archiv für Psychiatrie, etc., Vol. XXVI., No. 1, p. 1-130, reviewed in Centralblatt für Nervenheilkunde und Psychiatrie, XVIII., 1895, p. 610.

[8] Die Aetiologie der progressiven Paralyse. Jahrbücher für Psych., 14 Vol. iii., 1896, p. 321-541.

the cause of general paralysis, has, among other evidences, cited the results of an inquiry into a collection of cases with well-known tertiary lesions from Lang's clinic in Vienna, and has shown that there also, in spite of a most careful anamnesis, it was impossible to find a syphilitic history in all cases; indeed, taking everything into consideration, there was on this point a remarkable resemblance between general paralysis and tertiary syphilis. We must concede therefore, that even the possibility of all these cases being due to hereditary syphilis must be admitted, although this is not by any means proved, and surely never will be proved by any statistics. That our patients have such a heredity we cannot be certain, but we have seen that the father has had symptoms which were very suggestive.

There is one other point which it seems to me worth speaking of in this connection, and that is the differentiation of patients like ours from those which Homén described[9] as having a disease sui generis, most probably on the basis of a lues hereditaria tarda. The picture of our first patient reminded me at once very strongly of the clinical picture which Homén gives of his cases. We have here as there a disease occurring in more than one member of the same family, and here as there a progressive dementia; here as there, at least in one of our patients, contractures (although I have not seen the patient myself there can be no question about these, since I have received the same information from several members of the family independently). Homén also feels the necessity of distinguishing his cases from those of general paralysis, and the grounds on which he does it are the following: 1, the age; 2, the absence of any changes in the temper or disposition ("Laune"); 3, the absence of any delusions, and, 4, the absence of the characteristic speech disturbances. The first and third of these reasons at once prove valueless in view of our cases; nor can I see that the second, namely, the absence of changes in disposition, proves anything, not only because this certainly played an insignificant rôle in our cases, too, but because in the cases of demented forms of general paralysis this feature is less frequently seen than in the more classical pictures. The strongest point certainly is the absence of the characteristic speech-disturbances; a priori we should, however, owing to the fact that they, after all, do not depend on the disease process as such, but on the localization of it, assume that cases of general paralysis could occur without it, and we certainly know that such do occur. A good case in point, for example, is that reported by Lührmann,[10] also an instance of juvenile general paralysis. Here the symptom was lacking till death. We see, therefore, that for the present we have no sufficient data to separate the two diseases clinically. An entirely different question arises when we look at the pathological anatomical data. Here we find considerable differences. Homén found changes in the vessels which were very pronounced, not only in the brain, but in the other parts of the body as well; these he considers justly as the primary lesion. Moreover, it must strike us that the anatomical changes in Homén's cases are very slight in spite of the fact that the disease clinically was very profound and lasted for seven years in one instance; both the changes in the nerve cells and fibres and in the neuroglia were but slight. This also is, to my mind, a feature of great importance and one which points very strongly to a process which is essentially different from that of general paralysis. In other words, Homén's cases cannot be differentiated clinically from some cases of juvenile general paralysis, but anatomically they are essentially different.

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[9] Eine eigenthümliche, bei drei Geschwistern auftretende, typische Krankheit under der Form einer progressiven Demenz in Verbindung mit ausgedehnten Gefässveränderungen (wohl lues hereditaria tarda.) Arch. für Psych., Bd. xxiv., 1892, p. 191.

SUMMARY.

It is evident that the two sisters who were in apparently good health previous to the onset of their disease, gradually developed the symptoms of general paralysis, the one beginning at the age of ten, the other at the age of fifteen years. There is a neuropathic heredity, inasmuch as the father was prematurely senile, the mother very nervous. Besides, it is probable that the father has had lues and we have seen that a luetic heredity is very common in such cases.

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[10] Progressive Paralyse im jugendlichen Alter. Neurol. Centralblatt, 1895, p. 632.

The clinical course in both sisters was that of a simple progressive dementia, lasting in one case for six years, in the other so far for four years. We see from the literature that this simple demented form is the most common in these juvenile cases.

The autopsy in the younger sister proved the diagnosis. The lesions in the cerebral cortex were those commonly seen in general paralysis. Similar changes were found in the basal ganglia. In the cerebellar cortex was seen a more or less pronounced degeneration of many Purkinje cells with great increase in the neuroglia of the cortex and marked diminution in the thickness of the cortex. In the cord the anterior and lateral pyramids were affected. This degeneration could be followed into the pons, but was apparently lost in the crura. From the upper dorsal cord upward there was a degeneration in Gowers' tract, the field of degeneration becoming best marked in the high cervical region and the beginning of the medulla oblongata. This degeneration is probably due to changes in the gray matter of the cord which we find in the upper portions in the centre of the gray matter on either side. We have, finally, concluded that while we have every reason to regard the cases which Homén described as differing in their essential disease process from general paralysis, it may be impossible to differentiate the two diseases clinically.